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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JAN 02	STN pricing information for 2008 now available
NEWS	3	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS	4	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS	5	JAN 28	MARPAT searching enhanced
NEWS	6	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS	7	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS	8	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
NEWS	9	FEB 08	STN Express, Version 8.3, now available
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NEWS	11	FEB 25	IFIREF reloaded with enhancements
NEWS	12	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS	13	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification
NEWS	14	MAR 31	IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
NEWS	15	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS	16	MAR 31	CA/CAplus and CASREACT patent number format for U.S. applications updated
NEWS	17	MAR 31	LPCI now available as a replacement to LDPCI
NEWS	18	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	19	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS	20	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS	21	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS	22	APR 28	IMSRESEARCH reloaded with enhancements

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 15:12:25 ON 19 MAY 2008

=> File >gerry2MBCE
'>GERRY2MBCE' IS NOT A VALID FILE NAME
SESSION CONTINUES IN FILE 'HOME'
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available.  If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.

=> File .Gerry2mbce
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       1.68       1.68

FILE 'MEDLINE' ENTERED AT 15:16:58 ON 19 MAY 2008

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=> S Livin (S) apopto? AND pd<=20040531
   2 FILES SEARCHED...
L1          59 LIVIN (S) APOPTO? AND PD<=20040531

=> Dup Rem L1
PROCESSING COMPLETED FOR L1
L2          32 DUP REM L1 (27 DUPLICATES REMOVED)
               ANSWERS '1-12' FROM FILE MEDLINE
               ANSWERS '13-21' FROM FILE BIOSIS
               ANSWERS '22-32' FROM FILE CAPLUS

=> D Ti L2 1-32

L2   ANSWER 1 OF 32     MEDLINE on STN                  DUPLICATE 1
TI   CC chemokine ligand 25 enhances resistance to apoptosis in CD4+
     T cells from patients with T-cell lineage acute and chronic lymphocytic
     leukemia by means of livin activation.

L2   ANSWER 2 OF 32     MEDLINE on STN                  DUPLICATE 2
TI   The melanoma inhibitor of apoptosis protein: a target for spontaneous
     cytotoxic T cell responses.

L2   ANSWER 3 OF 32     MEDLINE on STN                  DUPLICATE 3
TI   Inhibition of apoptosis in normal and transformed intestinal epithelial
     cells by cAMP through induction of inhibitor of apoptosis protein (IAP)-2.

L2   ANSWER 4 OF 32     MEDLINE on STN                  DUPLICATE 4
TI   Induction of apoptosis in tumor cells by siRNA-mediated
     silencing of the livin/ML-IAP/KIAP gene.

L2   ANSWER 5 OF 32     MEDLINE on STN                  DUPLICATE 6
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TI Temporal and spatial patterns of expression of inhibitors of apoptosis in human placentas.

L2 ANSWER 6 OF 32 MEDLINE on STN DUPLICATE 7
TI Expression and prognostic significance of LIVIN, SURVIVIN and other apoptosis-related genes in the progression of superficial bladder cancer.

L2 ANSWER 7 OF 32 MEDLINE on STN DUPLICATE 8
TI Apoptosis regulators and responses in human melanocytic and keratinocytic cells.

L2 ANSWER 8 OF 32 MEDLINE on STN DUPLICATE 9
TI Expressed sequence tag analysis of adult human lens for the NEIBank Project: over 2000 non-redundant transcripts, novel genes and splice variants.

L2 ANSWER 9 OF 32 MEDLINE on STN DUPLICATE 10
TI Livin, a novel inhibitor of apoptosis protein family member.

L2 ANSWER 10 OF 32 MEDLINE on STN DUPLICATE 11
TI Two splicing variants of a new inhibitor of apoptosis gene with different biological properties and tissue distribution pattern.

L2 ANSWER 11 OF 32 MEDLINE on STN
TI Telomere-based DNA damage responses: a new approach to melanoma.

L2 ANSWER 12 OF 32 MEDLINE on STN
TI Expression of survivin mRNA and livin mRNA in non-small-cell lung cancer.

L2 ANSWER 13 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Expression of inhibitor-of-apoptosis protein livin by neuroblastoma cells: Correlation with stage of cellular maturation.

L2 ANSWER 14 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Livin, a novel member of inhibitor of apoptosis, is marker of poor prognosis in gastric cancer.

L2 ANSWER 15 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Livin, an inhibitor of apoptosis family member is a novel target for cancer immunotherapy.

L2 ANSWER 16 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Apoptotic cleavage of livin in melanoma cells.

L2 ANSWER 17 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Caspase-mediated cleavage paradoxically converts Livin from an anti-apoptotic to a pro-apoptotic factor: Implications for CLL, AML and drug resistant melanoma.

L2 ANSWER 18 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Apoptosis and melanoma: Molecular mechanisms.

L2 ANSWER 19 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

TI Differences in Gene Regulation among Members of the IAP Family in Response to Activation of Hematopoietic Cells.

L2 ANSWER 20 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Effector but Not Initiator Caspases Cleave the Inhibitor of Apoptosis Protein "Livin".

L2 ANSWER 21 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Livin, a new inhibitor of apoptosis protein, is expressed at high levels in some chronic lymphatic leukemia (CLL) patients, and may contribute to the apoptotic defect in low grade hematological malignancies.

L2 ANSWER 22 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 5
TI Livin - potential target for cancer treatment

L2 ANSWER 23 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Antisense modulation of livin expression

L2 ANSWER 24 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Peptides for inducing apoptosis in tumor cells

L2 ANSWER 25 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Smac/DIABLO Selectively Reduces the Levels of c-IAP1 and c-IAP2 but Not That of XIAP and Livin in HeLa Cells

L2 ANSWER 26 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Novel inhibitor of apoptosis: livin

L2 ANSWER 27 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Telomere-based DNA damage responses: a new approach to melanoma

L2 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Potent general cancer vaccines targeting inhibitor of apoptosis proteins

L2 ANSWER 29 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Rapid induction of mitochondrial events and caspase-independent apoptosis in Survivin-targeted melanoma cells

L2 ANSWER 30 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Methods and reagents for peptide-BIR interaction screens

L2 ANSWER 31 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Caspase-Mediated Cleavage Converts Livin from an Antiapoptotic to a Proapoptotic Factor: Implications for Drug-Resistant Melanoma

L2 ANSWER 32 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Protein and cDNA sequences of a novel human livin gene: inhibitor-of-apoptosis protein-3 (IAP-3) and its therapeutic uses

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SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 15:19:21 ON 19 MAY 2008

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SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE'
AT 15:21:50 ON 19 MAY 2008
FILE 'MEDLINE' ENTERED AT 15:21:50 ON 19 MAY 2008
FILE 'BIOSIS' ENTERED AT 15:21:50 ON 19 MAY 2008
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FULL ESTIMATED COST	14.15	15.83

=> D Hist

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     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:16:58 ON 19 MAY 2008
L1   59 S LIVIN (S) APOPTO? AND PD<=20040531
L2   32 DUP REM L1 (27 DUPLICATES REMOVED)

=> S L2 AND (p30 OR p28)
L3   0 L2 AND (P30 OR P28)

=> D ibib abs L2 1-32

L2   ANSWER 1 OF 32   MEDLINE on STN   DUPLICATE 1
ACCESSION NUMBER: 2004520941   MEDLINE
DOCUMENT NUMBER: PubMed ID: 15492285
TITLE: CC chemokine ligand 25 enhances resistance to
                    apoptosis in CD4+ T cells from patients with T-cell
                    lineage acute and chronic lymphocytic leukemia by means of
                    livin activation.
AUTHOR: Qiuping Zhang; Jei Xiong; Youxin Jin; Wei Ju; Chun Liu; Jin
                    Wang; Qun Wu; Yan Liu; Chunsong Hu; Mingzhen Yang; Qingping
                    Gao; Kejian Zhang; Zhimin Sun; Qun Li; Junyan Liu; Jinquan
                    Tan
CORPORATE SOURCE: Department of Immunology, and Laboratory of Allergy and
                    Clinical Immunology, Institute of Allergy and
                    Immune-related Diseases and Center for Medical Research,
                    Wuhan University School of Medicine, Wuhan, Republic of
                    China.
SOURCE: Cancer research, (2004 Oct 15) Vol. 64, No. 20,
                    pp. 7579-87.
                    Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 20 Oct 2004
                    Last Updated on STN: 19 Dec 2004
                    Entered Medline: 3 Dec 2004

AB We investigated CD4 and CD8 double-positive thymocytes, CD4(+) T cells from typical patients with T-cell lineage acute lymphocytic leukemia (T-ALL) and T cell lineage chronic lymphocytic leukemia (T-CLL), and MOLT4 T cells in terms of CC chemokine ligand 25 (CCL25) functions of induction of resistance to tumor necrosis factor alpha (TNF-alpha)-mediated apoptosis. We found that CCL25 selectively enhanced resistance to TNF-alpha-mediated apoptosis in T-ALL and T-CLL CD4(+) T cells as well as in MOLT4 T cells, but CD4 and CD8 double-positive thymocytes did not. One member protein of the inhibitor of apoptosis protein (IAP) family, Livin, was selectively expressed in the malignant cells at higher levels, particularly in T-ALL CD4(+) T cells, in comparison with the expression in CD4 and CD8 double-positive thymocytes. After stimulation with CCL25 and apoptotic induction with TNF-alpha, the expression levels of Livin in these malignant cells were significantly increased. CCL25/thymus-expressed chemokine (TECK), by means of CC chemokine receptor 9 (CCR9) ligation, selectively activated Livin to enhance resistance to TNF-alpha-mediated apoptosis in c-jun-NH(2)-kinase 1 (JNK1) kinase-dependent manner. These findings suggested differential functions of CCR9/CCL25 in distinct types of cells. CD4 and CD8 double-positive thymocytes used CCR9/CCL25 for migration, homing, development, maturation, selection, cell homeostasis, whereas malignant cells, particularly T-ALL CD4(+) T cells, used CCR9/CCL25 for infiltration, resistance to apoptosis, and inappropriate proliferation.

L2 ANSWER 2 OF 32 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004120007 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15009721
TITLE: The melanoma inhibitor of apoptosis protein: a target for spontaneous cytotoxic T cell responses.
AUTHOR: Andersen Mads Hald; Reker Sine; Becker Jurgen C; thor Straten Per
CORPORATE SOURCE: Tumor Immunology Group, Danish Cancer Society, Copenhagen, Denmark.. mha@cancer.dk
SOURCE: The Journal of investigative dermatology, (2004 Feb) Vol. 122, No. 2, pp. 392-9.
Journal code: 0426720. ISSN: 0022-202X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 11 Mar 2004
Last Updated on STN: 3 Apr 2004
Entered Medline: 2 Apr 2004

AB The identification of tumor antigens which expression is essential for the survival of tumor cells is a new avenue to prevent antigen loss variants emerging due to immunoselection, particularly during immune therapy. The melanoma inhibitor of apoptosis protein, ML-IAP (also named livin) counteracts apoptosis induced by death receptors, hypooxgenic conditions, or chemotherapeutic agents. Thus, elevated expression of ML-IAP renders melanoma cells resistant to apoptotic stimuli and thereby potentially contributes to the oncogenic phenotype. Here, we demonstrate that T cells in a large proportion of melanoma patients infiltrating the tumor or circulating in the peripheral blood specifically recognize ML-IAP-derived peptides. Interestingly, the responses against the peptide epitope ML-IAP280-289 were not restricted to melanoma patients but present among peripheral blood T cells in a few healthy controls. In situ peptide/HLA-A2 multimer staining, however, confirmed the infiltration of ML-IAP-reactive cells into the tumor microenvironment. Moreover, ML-IAP-reactive T cells isolated by magnetic beads coated with

peptide/HLA-A2 complexes were cytotoxic against HLA-matched melanoma cells. In conclusion, out data strongly indicate ML-IAP as a suitable target for immunologic intervention.

L2 ANSWER 3 OF 32 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2003344485 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12837940
TITLE: Inhibition of apoptosis in normal and transformed intestinal epithelial cells by cAMP through induction of inhibitor of apoptosis protein (IAP)-2.
AUTHOR: Nishihara Hiroshi; Kizaka-Kondoh Shinae; Insel Paul A; Eckmann Lars
CORPORATE SOURCE: Department of Pharmacology, University of California at San Diego, La Jolla, CA 92093, USA.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2003 Jul 22) Vol. 100, No. 15, pp. 8921-6. Electronic Publication: 2003-07-01. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 24 Jul 2003
Last Updated on STN: 3 Sep 2003
Entered Medline: 2 Sep 2003
AB Cyclooxygenase (COX)-2, a rate-limiting enzyme of prostaglandin (PG) production, is overexpressed in colorectal adenomas and adenocarcinomas, and its inhibition by nonsteroidal antiinflammatory drugs protects against colorectal cancer. Mechanisms of cancer promotion by COX-2 are not fully understood, but signaling through prostaglandin (PG)E2 receptors is a contributing factor. The major PGE2 receptors on epithelial cells, EP2 and EP4, increase cAMP production, which promotes growth and inhibits apoptosis in some cell types. Here, we show that cAMP agonists, including PGE2, cholera toxin, and a membrane-permeant cAMP analog, protect normal and transformed intestinal epithelial cells from apoptosis induced by diverse stimuli. This protection is associated with cAMP-mediated, rapid induction of cellular inhibitor of apoptosis protein (c-IAP)-2 and delayed induction of LIVIN, but not of six other members of the IAP family. Concurrently and characteristic of IAP functions, the activity, but not generation, of the cleaved form of the central executioner caspase 3 is inhibited. Induction of c-IAP2 expression by cAMP agonists is accompanied by phosphorylation of cAMP response element binding protein and cAMP response element-dependent activation of transcriptional reporters. Furthermore, inhibition of COX-2 in cells overexpressing the enzyme decreases c-IAP2 expression and promotes apoptosis, both of which are reversible by PGE2 addition, suggesting that COX-2-promoted antiapoptosis is mediated by release of PGE2 and subsequent cAMP-dependent c-IAP2 induction. These results help to explain the cancer chemoprotective effects of nonsteroidal antiinflammatory drugs by defining a mechanism through which cAMP signaling can promote the development of colorectal and possibly other epithelial cancers by means of disruption of normal apoptotic processes.

L2 ANSWER 4 OF 32 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2003541371 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14614456
TITLE: Induction of apoptosis in tumor cells by siRNA-mediated silencing of the livin/ML-IAP/KIAP gene.

AUTHOR: Crnkovic-Mertens Irena; Hoppe-Seyler Felix; Butz Karin
CORPORATE SOURCE: Angewandte Tumorvirologie, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 242, Heidelberg D-69120, Germany.
SOURCE: Oncogene, (2003 Nov 13) Vol. 22, No. 51, pp. 8330-6.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 19 Nov 2003
Last Updated on STN: 6 Jan 2004
Entered Medline: 5 Jan 2004

AB Increased resistance to apoptosis is a hallmark of many tumor cells. The functional inhibition of specific antiapoptotic factors may provide a rational basis for the development of novel therapeutic strategies. We investigated here whether the RNA interference (RNAi) technology could be used to increase the apoptotic susceptibility of cancer cells. As a molecular target, we chose the antiapoptotic livin (ML-IAP, KIAP) gene, which is expressed in a subset of human tumors. We identified vector-borne small interfering (si)RNAs, which could efficiently block endogenous livin gene expression. Silencing of livin was associated with caspase-3 activation and a strongly increased apoptotic rate in response to different proapoptotic stimuli, such as doxorubicin, UV-irradiation, or TNFalpha. The effects were specific for Livin-expressing tumor cells. Our results (i) provide direct evidence that the intracellular interference with livin gene expression resensitizes human tumor cells to apoptosis, (ii) define the livin gene as a promising molecular target for therapeutic inhibition, and (iii) show that the livin gene is susceptible to efficient and specific silencing by the siRNA technology.

L2 ANSWER 5 OF 32 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2003343750 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12875963
TITLE: Temporal and spatial patterns of expression of inhibitors of apoptosis in human placentas.
AUTHOR: Ka Hakhyun; Hunt Joan S
CORPORATE SOURCE: Department of Anatomy and Cell Biology, University of Kansas Medical Center, Kansas City, Kansas 66160, USA.
CONTRACT NUMBER: HD24212 (United States NICHD)
HD29156 (United States NICHD)
HD33994 (United States NICHD)
SOURCE: The American journal of pathology, (2003 Aug) Vol. 163, No. 2, pp. 413-22.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 24 Jul 2003
Last Updated on STN: 11 Sep 2003
Entered Medline: 10 Sep 2003

AB The apoptosis cascade that plays a central role in normal and pathological processes is strictly controlled, in part by newly described members of the inhibitor of apoptosis (IAP) family (HIAP-1, HIAP-2, XIAP, NAIP, Survivin, and Livin). Here, we report the

expression of IAP mRNAs and proteins in early and late gestation human placentas, term cytotrophoblast cells, and two choriocarcinoma cell lines, JEG-3 and Jar. Reverse transcriptase-polymerase chain reaction identified mRNAs derived from all of the currently known IAP genes in all samples. Analysis by immunoblotting revealed that IAP proteins are present in early and late gestation human placentas and that levels of IAPs are not identical in normal and transformed trophoblast cells. Immunohistochemical experiments performed on paraformaldehyde-fixed tissue sections taken from early and late stages of pregnancy demonstrated that expression patterns differed according to cell lineage and stage of cell differentiation. The results of this study are consistent with the postulate that IAP proteins have critical roles in placental cell survival and suggest that specific apoptosis inhibitors may protect normal and transformed trophoblast cells from cell death.

L2 ANSWER 6 OF 32 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2002725386 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12488298
TITLE: Expression and prognostic significance of LIVIN, SURVIVIN and other apoptosis-related genes in the progression of superficial bladder cancer.
AUTHOR: Gazzaniga P; Gradilone A; Giuliani L; Gandini O; Silvestri I; Nofroni I; Saccani G; Frati L; Agliano A M
CORPORATE SOURCE: Dipartimento di Medicina Sperimentale e Patologia, Universita degli Studi di Roma La Sapienza, Rome.
SOURCE: Annals of oncology : official journal of the European Society for Medical Oncology / ESMO, (2003 Jan) Vol. 14, No. 1, pp. 85-90.
Journal code: 9007735. ISSN: 0923-7534.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 19 Dec 2002
Last Updated on STN: 24 May 2003
Entered Medline: 23 May 2003

AB BACKGROUND: It has been suggested that progression of superficial bladder cancer may be regulated at the molecular level by a typical pattern of expression of genes involved in apoptosis. Recently LIVIN, belonging to the inhibitors of apoptosis (IAP) family, has been found to be expressed in most solid tumors, where its expression is suggested to have prognostic significance. No data are available concerning the significance of LIVIN in the progression of bladder tumors. PATIENTS AND METHODS: In the present paper we used RT-PCR to investigate the expression of LIVIN isoforms alpha and beta, SURVIVIN, BCL-X and BCL-2/BAX expression ratio both in normal and tumoral bladder tissues, and correlated their expression with the emergence of early relapses in a follow-up of 4 years. This study shows that only the alpha isoform of LIVIN, which is not expressed in normal bladder tissue, is expressed in a proportion of tumors with a high risk of relapse. RESULTS: LIVIN was found in 7/30 patients (23%), SURVIVIN in 9/30 (30%), BCL-2/BAX ratio >1 in 16/30 (53%), BCL-2/BAX expression ratio <1 in 14/30 (46.6%) and BCL-X, only in isoform BCL-X(L), in 11/30 (36.6%). When we evaluated the dependence between each gene expression and relapse free time of patients, we found that LIVIN, high BCL-2/BAX ratio and BCL-X(L), but not SURVIVIN, reached statistical significance in order to predict relapses. CONCLUSIONS: Our findings suggest that LIVIN may be involved in the progression of superficial bladder cancer and used as a marker of early recurrence; while the expression of SURVIVIN cannot be used to identify

patients with high risk of relapse.

L2 ANSWER 7 OF 32 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2003028614 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12535197
TITLE: Apoptosis regulators and responses in human melanocytic and keratinocytic cells.
AUTHOR: Bowen Anneli R; Hanks Adrianne N; Allen Sarah M; Alexander April; Diedrich Miyoung J; Grossman Douglas
CORPORATE SOURCE: Department of Dermatology, University of Utah, Salt Lake City, UT 84112, USA.
CONTRACT NUMBER: KO8AR48618 (United States NIAMS)
SOURCE: The Journal of investigative dermatology, (2003 Jan) Vol. 120, No. 1, pp. 48-55.
Journal code: 0426720. ISSN: 0022-202X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 22 Jan 2003
Last Updated on STN: 7 Feb 2003
Entered Medline: 6 Feb 2003

AB Apoptosis in keratinocytes is required for epidermal turnover, stratum corneum formation, and removal of ultraviolet-damaged premalignant cells. Its role in melanocyte homeostasis and transformation, on the other hand, has not been defined, although apoptosis resistance is a commonly recognized feature of melanoma. We examined the expression of apoptosis regulators in melanocytes, keratinocytes, melanoma, and HaCat cells. Melanocytic cells expressed relatively high levels of Bcl-2, Bcl-X(L), Mcl-1, C-IAP-1, C-IAP-2, XIAP, Livin, and Apaf-1. The only apoptotic regulator that was differentially expressed in melanoma cells and not melanocytes was Survivin, whereas Bax was expressed in melanocytes but not in most melanoma lines. Keratinocytic cells, on the other hand, expressed high levels of FLIP and were relatively deficient in Bcl-2 family proteins. Levels of p53 were highest in HaCat cells and some of the melanoma lines, and barely detectable in melanocytes and keratinocytes. Next, susceptibility of these cells types to apoptosis induced by ultraviolet B, the tyrosine analog 4-tert-butylphenol, and cytotoxic drugs was examined. Melanocytes were relatively resistant to ultraviolet B, whereas keratinocytes were unresponsive to 4-tert-butylphenol. Melanocytes and keratinocytes were generally less susceptible than melanoma lines and HaCat cells to etoposide, cisplatin, and staurosporine. Induction of apoptosis in these cell types was generally associated with decreased levels of Mcl-1, XIAP, and Livin, and increased levels of p53, whereas levels of other apoptotic regulators were unaltered. These results provide insights into the potential roles of apoptosis in the function and transformation of epidermal melanocytes and keratinocytes.

L2 ANSWER 8 OF 32 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2002365511 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12107413
TITLE: Expressed sequence tag analysis of adult human lens for the NEIBank Project: over 2000 non-redundant transcripts, novel genes and splice variants.
AUTHOR: Wistow Graeme; Bernstein Steven L; Wyatt M Keith; Behal Amita; Touchman Jeffrey W; Bouffard Gerald; Smith Don; Peterson Katherine
CORPORATE SOURCE: Section on Molecular Structure and Function, National Eye

Institute, National Institutes of Health, Bethesda, MD 20892-2740, USA.. graeme@helix.nih.gov
SOURCE: Molecular vision, (2002 Jun 15) Vol. 8, pp. 171-84. Electronic Publication: 2002-06-15. Journal code: 9605351. E-ISSN: 1090-0535.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: REFSEQ-NT_011333
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 12 Jul 2002
Last Updated on STN: 12 Dec 2002
Entered Medline: 16 Jul 2002

AB PURPOSE: To explore the expression profile of the human lens and to provide a resource for microarray studies, expressed sequence tag (EST) analysis has been performed on cDNA libraries from adult lenses. METHODS: A cDNA library was constructed from two adult (40 year old) human lenses. Over two thousand clones were sequenced from the unamplified, un-normalized library. The library was then normalized and a further 2200 sequences were obtained. All the data were analyzed using GRIST (GRouping and Identification of Sequence Tags), a procedure for gene identification and clustering. RESULTS: The lens library (by) contains a low percentage of non-mRNA contaminants and a high fraction (over 75%) of apparently full length cDNA clones. Approximately 2000 reads from the unamplified library yields 810 clusters, potentially representing individual genes expressed in the lens. After normalization, the content of crystallins and other abundant cDNAs is markedly reduced and a similar number of reads from this library (fs) yields 1455 unique groups of which only two thirds correspond to named genes in GenBank. Among the most abundant cDNAs is one for a novel gene related to glutamine synthetase, which was designated "lengsin" (LGS). Analyses of ESTs also reveal examples of alternative transcripts, including a major alternative splice form for the lens specific membrane protein MP19. Variant forms for other transcripts, including those encoding the apoptosis inhibitor Livin and the armadillo repeat protein ARVCF, are also described. CONCLUSIONS: The lens cDNA libraries are a resource for gene discovery, full length cDNAs for functional studies and microarrays. The discovery of an abundant, novel transcript, lengsin, and a major novel splice form of MP19 reflect the utility of unamplified libraries constructed from dissected tissue. Many novel transcripts and splice forms are represented, some of which may be candidates for genetic diseases.

L2 ANSWER 9 OF 32 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2001269973 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11024045
TITLE: Livin, a novel inhibitor of apoptosis protein family member.
AUTHOR: Kasof G M; Gomes B C
CORPORATE SOURCE: AstraZeneca Pharmaceuticals, Enabling Sciences and Technology, Wilmington, Delaware 19803, USA.
SOURCE: The Journal of biological chemistry, (2001 Feb 2) Vol. 276, No. 5, pp. 3238-46. Electronic Publication: 2000-10-09. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 25 Jun 2001

Last Updated on STN: 5 Jan 2003
Entered Medline: 21 Jun 2001

AB A novel human inhibitor of apoptosis protein (IAP) family member termed Livin was identified, containing a single baculoviral IAP repeat (BIR) domain and a COOH-terminal RING finger domain. The mRNA for livin was not detectable by Northern blot in most normal adult tissues with the exception of the placenta, but was present in developmental tissues and in several cancer cell lines. Highest levels were observed in two melanoma-derived cell lines, G361 and SK-Mel29. Transfection of livin in HeLa cells resulted in protection from apoptosis induced by expression of FADD, Bax, RIP, RIP3, and DR6. Similar to other IAP family members, the anti-apoptotic activity of Livin was dependent on the BIR domain. Livin was also capable of inhibiting DEVD-like caspase activity triggered by tumor necrosis factor-alpha. In vitro binding studies demonstrated a direct interaction between Livin and the active form of the downstream caspases, caspase-3 and -7, that was dependent on the BIR domain of Livin. In addition, the unprocessed and cleaved forms of caspase-9 co-immunoprecipitated with Livin in vivo, and recombinant Livin could inhibit the activation of caspase-9 induced by Apaf-1, cytochrome c, and dATP. The subcellular distribution of the transfected Livin was analyzed by immunofluorescence. Both Livin and Survivin were expressed in the nucleus and in a filamentous pattern throughout the cytoplasm. In contrast to the apoptotic activity, the COOH-terminal RING domain mediated its subcellular localization patterning. Further studies found that transfection of an antisense construct against livin could trigger apoptosis specifically in cell lines expressing livin mRNA. This was associated with an increase in DNA fragmentation and in DEVD-like caspase activity. Thus, disruption of Livin may provide a strategy to induce apoptosis in certain cancer cells.

L2 ANSWER 10 OF 32 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2001271909 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11322947
TITLE: Two splicing variants of a new inhibitor of apoptosis gene with different biological properties and tissue distribution pattern.
AUTHOR: Ashhab Y; Alian A; Polliack A; Panet A; Ben Yehuda D
CORPORATE SOURCE: Department of Hematology, Hadassah University Hospital, Ein-Karem, P.O. Box 12000, Jerusalem 91120, Israel.
SOURCE: FEBS letters, (2001 Apr 20) Vol. 495, No. 1-2, pp. 56-60.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 29 May 2001
Last Updated on STN: 25 Jun 2002
Entered Medline: 21 May 2001

AB Using homology searches, we identified a novel human inhibitor of apoptosis (IAP) gene. This gene has two splicing variants that contain open reading frames of 298 and 280 amino acids and both contained a single copy of baculovirus IAP repeat (BIR) and RING domain. We refer here to the longer and shorter variants as Livin alpha and beta, respectively. Semiquantitative reverse transcriptase-polymerase chain reaction demonstrated a tissue-specific and non-correlated expression pattern in both adult and fetal tissues. Both mRNA variants were detected in various transformed cell lines. Despite their very close similarity, the two isoforms have different antiapoptotic properties. Both isoforms have a

significant antiapoptotic activity in the Jurkat T cell line after triggering apoptosis via tumor necrosis factor and CD95 receptors. The Livin alpha but not beta protects cells from apoptosis induced by staurosporine, but in contrast, apoptosis initiated by etoposide was blocked only by the beta isoform. This difference in biological activities may indicate the presence of critical amino acids outside the BIR and RING domains. These functional and tissue distribution differences of Livin alpha and beta suggest that Livin may play a complex role in the regulation of apoptosis.

L2 ANSWER 11 OF 32 MEDLINE on STN
ACCESSION NUMBER: 2004435494 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15333580
TITLE: Telomere-based DNA damage responses: a new approach to melanoma.
AUTHOR: Puri Neelu; Eller Mark S; Byers H Randolph; Dykstra Sarah; Kubera John; Gilchrest Barbara A
CORPORATE SOURCE: Department of Dermatology, Boston University School of Medicine, Boston, Massachusetts 02118-2394, USA.
CONTRACT NUMBER: R03 AR050110-02 (United States NIAMS)
SOURCE: The FASEB journal : official publication of the Federation of American Societies for Experimental Biology, (2004 Sep) Vol. 18, No. 12, pp. 1373-81.
Journal code: 8804484. E-ISSN: 1530-6860.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 3 Sep 2004
Last Updated on STN: 6 Apr 2005
Entered Medline: 5 Apr 2005
AB Melanoma is the most fatal skin cancer, often highly resistant to chemotherapy. Here we show that treatment with an 11-base DNA oligonucleotide homologous to the telomere 3' overhang sequence (T-oligo) induces apoptosis of several established human melanoma cell lines, including the aggressive MM-AN line, whereas normal human melanocytes exposed to the same or higher T-oligo concentrations show only transient cell cycle arrest, implying that malignant cells are more sensitive to T-oligo effects. When MM-AN cells were briefly exposed to T-oligo in culture and injected into the flank or tail vein of SCID mice, eventual tumor volume and number of metastases were reduced 85-95% compared with control mice. Similarly, T-oligos administered intralesionally or systemically selectively inhibited the growth of previously established MM-AN tumor nodules in the flank and peritoneal cavity by 85 to 90% without detectable toxicity. We previously showed that T-oligos act through ATM, p95/Nbs1, E2F1, p16INK4A, p53, and the p53 homologue p73 to modulate downstream effectors and now additionally demonstrate striking down-regulation of the inhibitor of apoptosis protein livin/ML-IAP. We suggest that T-oligo mimics a physiologic DNA damage signal that is frequently masked in malignant cells and thereby activates innate cancer prevention responses. T-oligos may provide a novel therapeutic approach to melanoma.

L2 ANSWER 12 OF 32 MEDLINE on STN
ACCESSION NUMBER: 2004570176 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15541814
TITLE: Expression of survivin mRNA and livin mRNA in non-small-cell lung cancer.

AUTHOR: Tanabe Hiromi; Yagihashi Atsuhito; Tsuji Naoki; Shijubo Yasuharu; Abe Shosaku; Watanabe Naoki
CORPORATE SOURCE: Department of Clinical Laboratory Medicine, Sapporo Medical University School of Medicine, South-1, West-16, Chuo-ku, Sapporo 060 8543, Japan.
SOURCE: Lung cancer (Amsterdam, Netherlands), (2004 Dec) Vol. 46, No. 3, pp. 299-304.
Journal code: 8800805. ISSN: 0169-5002.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 16 Nov 2004
Last Updated on STN: 9 Mar 2005
Entered Medline: 8 Mar 2005

AB It has been suggested that suppression of apoptosis may contribute to the development and progression of cancer. Anti-apoptotic survivin and livin genes are highly expressed in cancer cells and transformed cells, but show little or no expression in normal differentiated tissues. However, there are no available data concerning livin expression in non-small-cell lung cancer (NSCLC). We therefore measured livin mRNA and survivin mRNA expression in 38 NSCLC cancer samples and 15 paired non-cancerous lung tissue samples using a quantitative reverse transcription-polymerase chain reaction (RT-PCR). While both mRNAs showed higher expression in cancers than non-cancerous tissues ($P < 0.001$), livin mRNA and survivin mRNA expression did not correlate with one another. When a cut-off value for positivity was set at the mean + S.D. for expression values in non-cancerous tissues, positivity rates for livin mRNA and survivin mRNA expression were 76.3% (29 of 38) and 36.8% (14 of 38) in lung cancers and 6.7% (1 of 15) and 0% (0 of 15), respectively, in paired non-cancerous lung tissue samples. Livin mRNA and survivin mRNA expression in tumors were up-regulated in 23 of 31 (74.2%) early-stage NSCLC patients and 11 of 31 (35.5%), respectively. Expression of both mRNAs in tumors varied independently of tumor histology. These results support the possibility that the livin gene may play a role in NSCLC development and increased expression of livin mRNA may serve as a new target for lung cancer treatment as well as survivin.

L2 ANSWER 13 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:256703 BIOSIS
DOCUMENT NUMBER: PREV200700278695
TITLE: Expression of inhibitor-of-apoptosis protein livin by neuroblastoma cells: Correlation with stage of cellular maturation.
AUTHOR(S): Kim, Dae-Kwang [Reprint Author]; Findley, Harry W.; Abramowsky, Carlos; Gu, Lubing; Zhou, Muxiang; Alvarado, Carlos S.
CORPORATE SOURCE: Emory Univ, Atlanta, GA 30322 USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (MAR 2004) Vol. 45, pp. 1007.
Meeting Info.: 95th Annual Meeting of the American-Association-for-Cancer-Research. Orlando, FL, USA. March 27 -31, 2004. Amer Assoc Canc Res.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Apr 2007
Last Updated on STN: 11 Jul 2007

L2 ANSWER 14 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:78553 BIOSIS
DOCUMENT NUMBER: PREV200600085294
TITLE: Livin, a novel member of inhibitor of apoptosis, is marker of poor prognosis in gastric cancer.
AUTHOR(S): Tu, ShuiPing; Chan, Annie O. O.; Lin, Marrie C. M.; Jiang, Xiaohua; Lam, S. K.; Kung, H. F.; Wong, Benjamin C. Y.
SOURCE: Gastroenterology, (APR 2004) Vol. 126, No. 4, Suppl. 2, pp. A456.
Meeting Info.: Digestive Disease Week/105th Annual Meeting of the American-Gastroenterological-Association. New Orleans, LA, USA. May 16 -20, 2004. Amer Gastroenterol Assoc.
CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Jan 2006
Last Updated on STN: 25 Jan 2006
AB Background: Livin/ML-IAP/K1AP, a novel member of IAP, is over-expressed in most cancer cells, but not, or to substantially lesser amounts in most normal adult tissues. Ectopic expression of Livin inhibits apoptosis induced by a variety of pro-apoptotic stimuli and mediates the drug-resistance in melanoma. In this study, we investigated the expression of Livin and its significance in human gastric cancer tissues. Method Thirty primary gastric cancer and 8 normal stomach mucosa tissue samples were obtained from Rujin Hospital, Shanghai Second Medical University, China. The mRNA and protein level of Livin and other IAP family proteins (survivin, XIAP and c-IAP-1 and c-IAP-2) were determined by RT-PCR and immunohistochemical staining, respectively CD31 staining was detected by immunohistochemical method. The extent of positive staining in the tumor area was graded as 1 + (10%), 2 + (11-50%) and 3 + (>50%). Results: The mRNA and protein level of Livin, survivin, XIAP, c-IAP-1 and c-IAP-2 were detected in all 4 gastric cancer cell lines used, as well as in 67.3%, 83.3%, 70%, 47% and 43% of gastric cancer patient tissues, respectively. In contrast, weak staining of Livin and survivin proteins were detected in only 25% and 37% normal gastric mucosa, respectively. Importantly, among members of the IAP family, only survivin and Livin protein levels display correlations with cancer cell differentiation, prognosis and survival. In reminiscent to that of survivin, Livin protein expression is positively correlated with poor differentiation ($p = 0.027$), and negatively with survival ($p = 0.006$, $r = -0.5$). In addition, Livin protein correlated negatively with that of survivin ($p = 0.05$, $r = -0.34$). Whereas survivin protein correlated positively with MVD ($p < 0.0001$, $r = 0.69$) and CD31 ($p = 0,046$, $r = 0.37$), and XIAP protein correlated negatively with that of survivin ($p = 0.009$, $r = -0.47$), CD31 ($p = 0.016$, $r = -0.44$) and MVD ($p = 0.038$, $r = -0.38$). Conclusion: Our results suggest that multiple IAP proteins are involved in stomach carcinogenesis and progress, and that Livin is potentially a new target for the diagnosis and treatment of gastric cancer.

L2 ANSWER 15 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:248409 BIOSIS
DOCUMENT NUMBER: PREV200400248301
TITLE: Livin, an inhibitor of apoptosis family member is a novel target for cancer immunotherapy.
AUTHOR(S): Kitamura, Hiroshi [Reprint Author]; Torigoe, Toshihiko [Reprint Author]; Hariu, Hiroyuki [Reprint Author]; Aketa,

Katsuyuki [Reprint Author]; Tamura, Yasuaki [Reprint Author]; Mano, Yoshinori [Reprint Author]; Nabeta, Chika [Reprint Author]; Nakanishi, Katsuya [Reprint Author]; Asanuma, Hiroko [Reprint Author]; Takahashi, Atsushi [Reprint Author]; Itoh, Naoki [Reprint Author]; Sato, Masaaki [Reprint Author]; Sato, Noriyuki [Reprint Author]; Tsukamoto, Taiji [Reprint Author]
CORPORATE SOURCE: Sapporo, Japan
SOURCE: Journal of Urology, (April 2004) Vol. 171, No. 4 Supplement, pp. 262. print.
Meeting Info.: Annual Meeting of the American Urological Association. San Francisco, CA, USA. May 08-13, 2004. American Urological Association.
CODEN: JOURAA. ISSN: 0022-5347.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 May 2004
Last Updated on STN: 6 May 2004

L2 ANSWER 16 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:319450 BIOSIS
DOCUMENT NUMBER: PREV200510114845
TITLE: Apoptotic cleavage of livin in melanoma cells.
AUTHOR(S): Brouha, B. [Reprint Author]; Liu, T.; Hanks, A.; Yan, H.; Grossman, D.
CORPORATE SOURCE: Univ Utah, Huntsman Canc Inst, Salt Lake City, UT USA
SOURCE: Journal of Investigative Dermatology, (MAR 2004) Vol. 122, No. 3, pp. A150.
Meeting Info.: 65th Annual Meeting of the Society-for-Investigative-Dermatology. Providence, RI, USA. April 28 -May 01, 2004. Soc Investigat Dermatol.
CODEN: JIDEAE. ISSN: 0022-202X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Aug 2005
Last Updated on STN: 25 Aug 2005

L2 ANSWER 17 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:151252 BIOSIS
DOCUMENT NUMBER: PREV200400147482
TITLE: Caspase-mediated cleavage paradoxically converts Livin from an anti-apoptotic to a pro-apoptotic factor: Implications for CLL, AML and drug resistant melanoma.
AUTHOR(S): Nachmias, Boaz [Reprint Author]; Ashhab, Yaqoub [Reprint Author]; Bucholtz, Vered [Reprint Author]; Ben-Yehuda, Dina [Reprint Author]
CORPORATE SOURCE: Department of Hematology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 587a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)

Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB Inhibitor of Apoptosis Proteins (IAP) are a family of intracellular proteins that play an essential role in the regulation of apoptosis. IAP family members are defined by one or more repeats of a highly conserved 70 amino acids domain termed the baculovirus IAP repeat (BIR), located at the amino-terminal. With the exception of NIAP and Survivin, human IAPs also contain a conserved sequence termed RING finger at the carboxy-terminal. In a previous study we have identified IAP family member Livin and demonstrated that it has two splicing variants, Livin alpha and beta. Livin has a single BIR domain and a carboxy-terminal RING finger motif, and is able to inhibit apoptosis induced by a variety of stimuli. Recently we have demonstrated that following apoptotic stimuli, Livin is cleaved by effector caspases 3 and 7. In our current study we further analyzed the functional significance of the cleavage. Using site directed mutagenesis we mapped the cleavage site to aspartic acid 52. Cleavage at this point produces a large sub-unit with both the BIR and RING domains, and a small N-terminal fragment. Strikingly, the cleaved Livin, though containing intact BIR and RING domains, does not only lose its anti-apoptotic function, but actually gains, a pro-apoptotic effect. Transient expression of the subunit in 293 T cells and in LB33-Mel A1, a melanoma cell line, produced marked spontaneous apoptosis. Furthermore, 721.221 EBV-transformed B cells stably expressing the subunit showed a higher rate of apoptosis following treatment with anti CD95/Fas. Using deletion mutants we were able to determine that both the exposed area immediately distal to the cleavage site and the RING domain are critical for the pro-apoptotic effect. Livin inhibits apoptosis mainly through direct binding and inhibition of caspases. This study reveals that the downstream caspases cleave Livin to produce a pro-apoptotic subunit. We suggest that the balance between caspase activity and Livin expression determines whether Livin inhibits or further propagates apoptosis through its cleavage. In order to explore the clinical relevance of Livin, we used RT-PCR to determine Livin levels in samples from 28 pts with CLL and found correlation between high CD38 levels and high Livin expression. In 24 patients with AML we demonstrated high level of Livin expression in 9/10 pts with M2 and in only 3 out of 7 pts with APL. Our studies further explored the role of Livin and its regulatory mechanism in primary cultures derived from pts with metastatic melanoma. Livin expression was variable among the different pts, in contrast to uniform expression of other inhibition of apoptosis proteins such as XIAP and Survivin. Notably, we demonstrated that the expression level of Livin was directly correlated with chemotherapy sensitivity in vitro, and with the clinical response of the patient.

L2 ANSWER 18 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:173859 BIOSIS
DOCUMENT NUMBER: PREV200300173859
TITLE: Apoptosis and melanoma: Molecular mechanisms.
AUTHOR(S): Hussein, Mahmoud R.; Haemel, Anna K.; Wood, Gary S. [Reprint Author]
CORPORATE SOURCE: Department of Dermatology, University of Wisconsin, One South Park, 7th Floor, Madison, WI, 53715, USA
gsw@medicine.wisc.edu
SOURCE: Journal of Pathology, (March 2003) Vol. 199, No. 3, pp. 275-288. print.
ISSN: 0022-3417 (ISSN print).
DOCUMENT TYPE: Article

General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Apr 2003
Last Updated on STN: 2 Apr 2003

AB Melanoma cells can undergo self-destruction via programmed cell death, i.e. apoptosis. In these tumours, the molecular components of apoptosis include positive (apoptotic) and negative (anti-apoptotic) regulators. The former include p53, Bid, Noxa, PUMA, Bax, TNF, TRAIL, Fas/FasL, PITSLRE, interferons, and c-KIT/SCF. The latter include Bcl-2, Bcl-XL, Mcl-1, NF-KB, survivin, livin, and ML-IAP. Alternatively, some molecules such as TRAF-2, c-Myc, endothelins, and integrins may have either pro- or anti-apoptotic effects. Some of these molecules are of potential therapeutic use, such as: (1) p53, which influences resistance to chemotherapy; (2) Mcl-1 and Bcl-XL, which can override apoptosis; (3) TRAIL, which has selective fatal effects on tumour cells; (4) NF-KB, which when downregulated sensitizes cells to TRAIL and TNF; (5) the PITSLRE kinases, whose alteration appears to result in Fas resistance; (6) interferons, which sensitize cells to other factors; and (7) survivin and other IAPs that inhibit apoptosis. This review summarizes the state of current knowledge about the key molecular components and mechanisms of apoptosis in melanoma, discusses potential therapeutic ramifications, and provides directions for future research.

L2 ANSWER 19 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:367701 BIOSIS
DOCUMENT NUMBER: PREV200300367701
TITLE: Differences in Gene Regulation among Members of the IAP Family in Response to Activation of Hematopoietic Cells.
AUTHOR(S): Bucholtz, Vered [Reprint Author]; Ashhab, Yaqoub [Reprint Author]; Nachmias, Boaz [Reprint Author]; Ben-Yehuda, Dina [Reprint Author]
CORPORATE SOURCE: Hematology, Hadassah University Hospital, Jerusalem, Israel
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp.
Abstract No. 4217. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Aug 2003
Last Updated on STN: 13 Aug 2003

AB The Inhibitor of Apoptosis Proteins (IAP) are a family of proteins known to play a crucial role in inhibiting caspases, the central components of apoptotic pathways. To date, eight members of the IAP family have been identified in humans: XIAP, ILP2, cIAP1, cIAP2, NIAP, BRUCE, Survivin, and the new member, Livin, which was recently described by us and others. In addition to inhibition of apoptosis, some of these proteins were found to be involved in other cellular activities, such as regulation of the cell cycle. So far, little is known about the expression profiles of IAPs in different hematopoietic cell lineages. The goal of this work was to determine the expression patterns of the genes encoding for Livin, XIAP and Survivin in highly purified populations of mononuclear cells. In addition, we investigated the transcription regulation of these genes by comparing the expression levels before and after cell activation. The cDNA panel of highly purified cell fractions (purchased from Clontech) included the following populations, all in the resting and activated states: mixed mononuclear cells, CD4+, CD8+, and CD19+ cells, and resting CD14+ cells. To ensure equal input, the cDNAs were normalized using

semiquantitative RT-PCR for the house-keeping genes beta-actin and GAPDH . Gene-specific primers were used to assess the expression levels of Livin, XIAP and Survivin. High levels of both Livin and XIAP were found in the resting CD14+, CD4+, CD8+, CD19+ cells as well as in the mixed mononuclear cells. On the other hand, cDNAs of the activated counterparts showed lower levels of these transcripts. In contrast to Livin and XIAP, Survivin predominantly showed increased expression following cell activation. Our findings of higher Survivin levels after cell activation are compatible with recently published data showing upregulation of this gene following activation of various mononuclear cells. This concurs with the observation that Survivin shows a cell cycle-dependent expression, which is enhanced at the G2/M phase. Our novel observation of decreased expression of Livin and XIAP may explain the phenomenon of increased susceptibility to apoptosis described in activated mononuclear cells. Further investigation is required to explore the physiological significance of the differences in gene regulation among members of the IAP family in hematopoietic cells. In conclusion, our results may indicate a similar transcription regulation pattern for Livin and XIAP which is distinct from that of Survivin.

L2 ANSWER 20 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:335767 BIOSIS
DOCUMENT NUMBER: PREV200300335767
TITLE: Effector but Not Initiator Caspases Cleave the Inhibitor of Apoptosis Protein "Livin".
AUTHOR(S): Nachmias, Boaz [Reprint Author]; Ashhab, Yaqoub [Reprint Author]; Bucholtz, Vered [Reprint Author]; Ben-Yehuda, Dina [Reprint Author]
CORPORATE SOURCE: Hematology, Hadassah University Hospital, Jerusalem, Israel
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 1167. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003

AB Inhibitor of Apoptosis Proteins (IAP) are a family of intracellular proteins that play an essential role in the regulation of the apoptotic process. Recently, we and others discovered a new member of this group. The gene, designated Livin, encodes two splicing variants termed Livin alpha and beta. IAP members inhibit apoptosis primarily by their direct binding and inhibition of caspases, a group of cell-death proteases. Many studies have focused on the effect of IAPs on caspases. In the present work we explored the effect of various caspases on Livin isoforms. Using retroviral infection, we have established a Jurkat T cell line and an EBV-transformed B cell line 721.221 that express high, stable levels of either Livin alpha or beta. After treating the cells with one of the following apoptosis inducers: staurosporine, etoposide or Fas ligand, whole cell extracts were analyzed by Western blot using a polyclonal antibody that recognizes both isoforms. We found that upon the induction of apoptosis, both Livin alpha and beta underwent at least one site-specific cleavage, producing detectable fragments of 30kD and 28kD, respectively. The cleavage process increased over time and was observed prior to the detection of a significant percentage of apoptosis using Annexin-V staining. Notably, the Livin alpha cleaved fragment was detected earlier than that of Livin beta. To determine whether the

cleavage is mediated by caspases, we used a pan-caspase inhibitor zVAD-FMK. Pre-incubation with this inhibitor diminished cleavage of both Livin isoforms in a dose-dependent manner. Moreover, in vitro assays showed that effector caspsases 3, 6 and 7, but not initiator caspases 8 and 9, were able to cleave Livin. These findings suggest a novel bidirectional molecular interaction between Livin and various caspases. We speculate that the cleavage of Livin by certain caspases serves as a positive feedback mechanism to overcome the anti-apoptotic barrier posed by Livin during cell death. We are currently in the process of determining the specific site of cleavage and its regulatory aspects.

L2 ANSWER 21 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:153092 BIOSIS
DOCUMENT NUMBER: PREV200200153092
TITLE: Livin, a new inhibitor of apoptosis protein, is expressed at high levels in some chronic lymphatic leukemia (CLL) patients, and may contribute to the apoptotic defect in low grade hematological malignancies.
AUTHOR(S): Ashhab, Yaqoub [Reprint author]; Alian, Akram; Polliack, Aaron [Reprint author]; Zelig, Orly [Reprint author]; Panet, Amos; Yehuda, Dina Ben [Reprint author]
CORPORATE SOURCE: Hematology, Hadassah University Hospital, Jerusalem, Israel
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 151a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Feb 2002
Last Updated on STN: 4 Apr 2002

AB The inhibitor of apoptosis proteins (IAPs) are novel family of intracellular proteins which suppress apoptosis induced by a variety of stimuli. To date five members of the IAP family of proteins have been identified in humans; HIAP1, HIAP2, XIAP, NIAP, and Survivin. Using homology searches, we and others identified a novel human inhibitor of apoptosis gene named Livin. Our study revealed the existence of two splice variants of this gene that contain open reading frames of 298 and 280 amino acids and both contain a single copy of the BIR and RING domains. We refer to the longer and shorter variants as Livin alpha and beta, respectively. The two variants showed tissue specific expression patterns in both adult and fetal tissues. We demonstrated that both isoforms have significant antiapoptotic activity in Jurkat T cell lymphoma cells after triggering apoptosis via TNF and CD95 receptors. The Livin alpha but not beta isoform protects cells from apoptosis induced by Staurosporine, but in contrast, apoptosis initiated by Etoposide was blocked only by the beta isoform. These functional and tissue distribution differences of Livin alpha and beta suggest that Livin may play a complex role in the regulation of apoptosis. We used RT-PCR to test the expression levels of Livin in 17 samples of CLL patients as well as 12 lymphoma and leukemia cell lines. High levels of Livin were detected in 8/17 CLL samples, but only in 1/6 peripheral blood sample of healthy controls. In CLL, Survivin and XIAP levels were low. In contrast to Livin, in healthy controls, high levels of Survivin and XIAP were found. Among hematological cell lines, high levels of Livin were found

only in K562 and HL-60. In other cell lines, the levels were either low or undetectable. On the other hand, the levels of Survivin were high in all the cell lines, while XIAP was almost undetectable. These results suggest a possible association between high levels of Livin and the defect in the apoptotic process in B-CLL, which renders the cells resistant to chemotherapy. These findings may shed light on the variability of the clinical course in CLL. Furthermore, they may yield valuable insights that have important treatment implications for the use of specific agents in this disease. We are now in the process of developing advanced techniques to study the association between Livin expression and apoptosis defects in CLL and other hematological malignancies.

L2 ANSWER 22 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2004:1103173 CAPLUS
DOCUMENT NUMBER: 142:273156
TITLE: Livin - potential target for cancer treatment
AUTHOR(S): Zhang, Huadong; Yuan, Shoujun; Chen, Huipeng
CORPORATE SOURCE: Dept of Pharmacology, Institute of Radiation Medicine, Academy of Military Medical Sciences, Beijing, 100850, Peop. Rep. China
SOURCE: Zhongguo Yaolixue Tongbao (2003), 19(8), 845-847
CODEN: ZYTOE8; ISSN: 1001-1978
PUBLISHER: Anhui Yike Daxue Linchuan Yaoli Yanjiuso
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 9 refs. on livin potential target for cancer treatment with subdivision headings: (1) livin structure and its distribution characteristics; (2) the relation between livin and cancer; (3) the mechanism of effects of livin; (4) possibility of livin being a new target for cancer treatment and summary.

L2 ANSWER 23 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:18794 CAPLUS
DOCUMENT NUMBER: 140:105313
TITLE: Antisense modulation of livin expression
INVENTOR(S): Bennett, C. Frank; Dobie, Kenneth W.
PATENT ASSIGNEE(S): Isis Pharmaceuticals Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 60 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 17
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040005565	A1	20040108	US 2002-188646	20020702 <--
WO 2004005554	A2	20040115	WO 2003-US20821	20030702 <--
WO 2004005554	A3	20040304		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003247701	A1	20040123	AU 2003-247701	20030702 <--

US 20050164254 A1 20050728 US 2004-10227 20041209
PRIORITY APPLN. INFO.: US 2002-173240 B2 20020614
US 2002-188646 A 20020702
US 2002-213796 A2 20020806
US 2002-298354 A2 20021116
US 2002-300424 A2 20021119
US 2002-303326 A2 20021121
US 2002-303587 A2 20021121
US 2002-303325 A2 20021122
US 2002-303266 A2 20021123
US 2002-316244 A2 20021210
US 2002-316540 B2 20021210
US 2002-317248 A2 20021210
US 2002-317253 B2 20021210
US 2002-317272 A2 20021210
US 2002-317273 A2 20021210
US 2002-317280 A2 20021210
WO 2003-US20821 W 20030702

AB Antisense compds., compns. and methods are provided for modulating the expression of Livin. The compns. comprise antisense compds., particularly antisense oligonucleotides, targeted to nucleic acids encoding Livin. Methods of using these compds. for modulation of Livin expression and for treatment of diseases associated with expression of Livin are provided.

L2 ANSWER 24 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:17422 CAPLUS
DOCUMENT NUMBER: 140:87670
TITLE: Peptides for inducing apoptosis in tumor cells
INVENTOR(S): Butz, Karin; Crnkovic-Mertens, Irena; Hoppe-Seyler, Felix; Rausch, Christian
PATENT ASSIGNEE(S): Deutsches Krebsforschungszentrum Stiftung des Offentlichen Rechts, Germany
SOURCE: Eur. Pat. Appl., 46 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1378515	A1	20040107	EP 2002-14074	20020701 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
WO 2004003008	A2	20040108	WO 2003-EP6958	20030701 <--
WO 2004003008	A3	20040401		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003249912	A1	20040119	AU 2003-249912	20030701 <--
EP 1523495	A2	20050420	EP 2003-761567	20030701
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
EP 1795538	A1	20070613	EP 2006-122212	20030701
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,				

IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR
US 20050203288 A1 20050915 US 2005-519539 20050315
PRIORITY APPLN. INFO.: EP 2002-14074 A 20020701
EP 2003-761567 A3 20030701
WO 2003-EP6958 W 20030701
AB The invention discloses peptides which interact with IAPs (inhibitor of apoptosis proteins). IAPs are highly expressed in tumor cells which fail to undergo apoptosis. By binding to IAPs, the peptides of the invention release tumor cells from the apoptosis block and thus provide a new tool for effective cancer therapy.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 25 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:325326 CAPLUS
DOCUMENT NUMBER: 140:336249
TITLE: Smac/DIABLO Selectively Reduces the Levels of c-IAP1 and c-IAP2 but Not That of XIAP and Livin in HeLa Cells
AUTHOR(S): Yang, Qi-Heng; Du, Chunying
CORPORATE SOURCE: Stowers Institute for Medical Research, Kansas City, MO, 64110, USA
SOURCE: Journal of Biological Chemistry (2004), 279(17), 16963-16970
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The inhibitor of apoptosis (IAP) proteins bind and inhibit caspases via their baculovirus IAP repeat domains. Some of these IAPs are capable of ubiquitinating themselves and their interacting proteins through the ubiquitin-protein isopeptide ligase activity of their RING domain. The Drosophila IAP antagonists Reaper, Hid, and Grim can accelerate the degradation of Drosophila IAP1 and some mammalian IAPs by promoting their ubiquitin-protein isopeptide ligase activity. Here we show that Smac/DIABLO, a mammalian functional homolog of Reaper/Hid/Grim, selectively causes the rapid degradation of c-IAP1 and c-IAP2 but not XIAP and Livin in HeLa cells, although it efficiently promotes the auto-ubiquitination of them all. Smac binding to c-IAP via its N-terminal IAP-binding motif is the prerequisite for this effect, which is further supported by the findings that Smac N-terminal peptide is sufficient to enhance c-IAP1 ubiquitination, and Smac no longer promotes the ubiquitination of mutant c-IAP1 lacking all three baculovirus IAP repeat domains. In addition, different IAPs require the same ubiquitin-conjugating enzymes UbcH5a and UbcH6 for their ubiquitination. Taken together, Smac may serve as a key mol. in vivo to selectively reduce the protein level of c-IAPs through the ubiquitin/proteasome pathway.
REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 26 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:164475 CAPLUS
DOCUMENT NUMBER: 143:4890
TITLE: Novel inhibitor of apoptosis: livin
AUTHOR(S): Zhen, Haining; Zhang, Xiang
CORPORATE SOURCE: Xijing Hospital, Fourth Military Medical University, Xian, Shanxi Province, 710033, Peop. Rep. China
SOURCE: Disi Junyi Daxue Xuebao (2004), 25(19), 1822-1823
CODEN: DJDXEG; ISSN: 1000-2790
PUBLISHER: Disi Junyi Daxue Xuebao Bianjibu

DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review introduces a novel member of inhibitor of apoptosis protein (IAP), livin, with the mol. biol. characteristics, the effects of anti-apoptosis, signal transduction, the mechanism of regulation, expression in normal tissues and the relation with neoplasm, etc.

L2 ANSWER 27 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:742120 CAPLUS
DOCUMENT NUMBER: 141:405770
TITLE: Telomere-based DNA damage responses: a new approach to melanoma
AUTHOR(S): Puri, Neelu; Eller, Mark S.; Byers, H. Randolph; Dykstra, Sarah; Kubera, John; Gilchrest, Barbara A.
CORPORATE SOURCE: Department of Dermatology, Boston University School of Medicine, Boston, MA, 02118-2394, USA
SOURCE: FASEB Journal (2004), 18(12), 1372-1381, 10.1096/fj.04-1774com
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Melanoma is the most fatal skin cancer, often highly resistant to chemotherapy. Here we show that treatment with an 11-base DNA oligonucleotide homologous to the telomere 3' overhang sequence (T-oligo) induces apoptosis of several established human melanoma cell lines, including the aggressive MM-AN line, whereas normal human melanocytes exposed to the same or higher T-oligo concns. show only transient cell cycle arrest, implying that malignant cells are more sensitive to T-oligo effects. When MM-AN cells were briefly exposed to T-oligo in culture and injected into the flank or tail vein of SCID mice, eventual tumor volume and number of metastases were reduced 85-95% compared with control mice. Similarly, T-oligos administered intralesionally or systemically selectively inhibited the growth of previously established MM-AN tumor nodules in the flank and peritoneal cavity by 85 to 90% without detectable toxicity. We previously showed that T-oligos act through ATM, p95/Nbs1, E2F1, p16INK4A, p53, and the p53 homolog p73 to modulate downstream effectors and now addnl. demonstrate striking down-regulation of the inhibitor of apoptosis protein livin/ML-IAP. We suggest that T-oligo mimics a physiol. DNA damage signal that is frequently masked in malignant cells and thereby activates innate cancer prevention responses. T-oligos may provide a novel therapeutic approach to melanoma.
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:627960 CAPLUS
DOCUMENT NUMBER: 142:238017
TITLE: Potent general cancer vaccines targeting inhibitor of apoptosis proteins
AUTHOR(S): Hariu, Hiroyuki; Yamamoto, Masaaki; Torigoe, Toshihiko
CORPORATE SOURCE: Department of Pathology, Sapporo Medical University School of Medicine, Sapporo, 060-8556, Japan
SOURCE: Rinsho Men'eki (2004), 41(4), 379-384
CODEN: RNMKAU; ISSN: 0386-9695
PUBLISHER: Kagaku Hyoronsha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review discusses role of inhibitor of apoptosis proteins

including survivin and livin as antigen for target of tumor vaccine.

L2 ANSWER 29 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:88623 CAPLUS
DOCUMENT NUMBER: 140:161512
TITLE: Rapid induction of mitochondrial events and caspase-independent apoptosis in Survivin-targeted melanoma cells
AUTHOR(S): Liu, Tong; Brouha, Brook; Grossman, Douglas
CORPORATE SOURCE: Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, 84112, USA
SOURCE: Oncogene (2004), 23(1), 39-48
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The inhibitor of apoptosis (IAP) protein Survivin is expressed in most cancers and is a key factor in maintaining apoptosis resistance. Although several IAPs have been shown to act as direct inhibitors of caspases, the precise antiapoptotic function of Survivin remains controversial. To clarify the mechanism by which Survivin protects cells, the authors investigated the kinetics of apoptosis and apoptotic events following Survivin inhibition utilizing a melanoma cell line harboring a tetracycline-regulated Survivin dominant-neg. mutant (Survivin-T34A). Blocking Survivin resulted in both caspase activation and apoptosis; however, the level of apoptosis was only partially reduced by caspase inhibition. Survivin blockade also resulted in mitochondrial events that preceded caspase activation, including depolarization and release of cytochrome c and Smac/DIABLO. Levels of other IAPs were not altered in Survivin-targeted cells, although modest cleavage of XIAP and Livin was observed The earliest proapoptotic event observed in Survivin-targeted cells was nuclear translocation of mitochondrial apoptosis-inducing factor (AIF), known to trigger both apoptotic mitochondrial events and caspase-independent DNA fragmentation. These findings suggest that a key antiapoptotic function of Survivin relates to inhibition of mitochondrial and AIF-dependent apoptotic pathways, and its expression in melanoma and other cancers likely protects against both caspase-independent and -dependent apoptosis.
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 30 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:376888 CAPLUS
DOCUMENT NUMBER: 138:379183
TITLE: Methods and reagents for peptide-BIR interaction screens
INVENTOR(S): Boudreault, Alain; Korneluk, Robert G.; La Casse, Eric; Liston, Peter
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040172	A2	20030515	WO 2002-CA1738	20021112 <--
WO 2003040172	A3	20040311		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002339280	A1	20030519	AU 2002-339280		20021112 <--
US 20030157522	A1	20030821	US 2002-293371		20021112 <--
PRIORITY APPLN. INFO.:			US 2001-332300P	P	20011109
			US 2002-370934P	P	20020408
			WO 2002-CA1738	W	20021112

AB The invention features a substantially pure polypeptide having a length of less than 100 amino acids and capable of forming a complex with a polypeptide that includes a BIR domain. The invention also features displacement assays in which the ability of a candidate compound to disrupt the interaction between a BIR domain-containing polypeptide and a polypeptide of the invention is indicative of the ability of the candidate compound to modulate IAP biol. activity.

L2 ANSWER 31 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:809098 CAPLUS
DOCUMENT NUMBER: 140:122305
TITLE: Caspase-Mediated Cleavage Converts Livin from an Antiapoptotic to a Proapoptotic Factor: Implications for Drug-Resistant Melanoma
AUTHOR(S): Nachmias, Boaz; Ashhab, Yaqoub; Bucholtz, Vered; Drize, Olga; Kadouri, Luna; Lotem, Michal; Peretz, Tamar; Mandelboim, Ofer; Ben-Yehuda, Dina
CORPORATE SOURCE: The Lautenberg Center for General and Tumor Immunology, Hadassah University Hospital, Department of Hematology, Hebrew University-Hadassah Medical School, Jerusalem, 91120, Israel
SOURCE: Cancer Research (2003), 63(19), 6340-6349
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Inhibitor of apoptosis protein (IAP) is a family of intracellular proteins that plays an essential role in the regulation of apoptosis. Recently, we and others discovered a new member of this family, termed Livin. Many studies have focused on the inhibitory effect of IAPs on caspases. Here, we describe a novel regulatory mechanism by which Livin is cleaved by the caspases. Strikingly, the cleaved Livin, although containing intact baculovirus IAP repeat and RING domains, does not only lose its antiapoptotic function but also gains a proapoptotic effect. The cleavage is site specific at Asp-52 and is restricted to effector caspase-3 and -7. Most importantly, we demonstrate the role of Livin and this regulatory mechanism in the drug resistance of melanoma patients. Using primary cultures derived from melanoma patients, we found a correlation between Livin overexpression, in vitro drug resistance, and the patient's clin. response.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 32 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:900802 CAPLUS
DOCUMENT NUMBER: 134:52288
TITLE: Protein and cDNA sequences of a novel human livin gene: inhibitor-of-apoptosis

protein-3 (IAP-3) and its therapeutic uses
INVENTOR(S): Gomes, Bruce Charles; Kasof, Garrett Mitchell; Prosser, Judith Caroline
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077201	A1	20001221	WO 2000-GB2272	20000609 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 20030087319	A1	20030508	US 2002-244586	20020916 <--
US 7183396	B2	20070227		

PRIORITY APPLN. INFO.: US 1999-139291P P 19990615
US 2000-594119 A1 20000614

AB The invention provides protein and cDNA sequences of a novel human gene for IAP-3, termed livin which is a member of the inhibitor-of-apoptosis protein (IAPs) family. The full-length cDNA of IAP-3 gene is 1376bp and its encoded protein has 280 amino acid. Livin contains a BIR domain (amino acid 87-154, critical motif for IAP protein anti-apoptotic activity and interaction with caspases) and a RING domain (amino acid 249-258). The protein sequence similarity of livin to other IAP family members are presented. Studies show that livin suppresses apoptosis induced by multiple stimuli, and antisense livin mol. can induce apoptosis. In addition, livin inhibits caspase activity and binds to caspase-3, -7, and -9. Methods of expression and preparation of livin and its antibody are described. The invention further relates to the uses of IAP-3 gene for drug screening for apoptosis relates disorders. Biol.-effective antisense mols. as well as dominant neg. mutant versions of the livin protein which are suitable for therapeutic are also provided. The invention is also drawn toward the study, prevention, diagnosis, and treatment of pathophysiol. disorders related to apoptosis.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 15:23:01 ON 19 MAY 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:

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 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE'
AT 17:05:58 ON 19 MAY 2008
FILE 'MEDLINE' ENTERED AT 17:05:58 ON 19 MAY 2008
FILE 'BIOSIS' ENTERED AT 17:05:58 ON 19 MAY 2008
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FILE 'CAPLUS' ENTERED AT 17:05:58 ON 19 MAY 2008
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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      75.00      76.68

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -8.80      -8.80

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     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:16:58 ON 19 MAY 2008
L1            59 S LIVIN (S) APOPTO? AND PD<=20040531
L2            32 DUP REM L1 (27 DUPLICATES REMOVED)
L3             0 S L2 AND (P30 OR P28)

=> S Livin(S) Apopto?
L4           243 LIVIN(S) APOPTO?

=> Dup Rem L4
PROCESSING COMPLETED FOR L4
L5           133 DUP REM L4 (110 DUPLICATES REMOVED)
                 ANSWERS '1-46' FROM FILE MEDLINE
                 ANSWERS '47-61' FROM FILE BIOSIS
                 ANSWERS '62-127' FROM FILE CAPLUS
                 ANSWERS '128-133' FROM FILE EMBASE

=> D Ti L5 1-133

L5   ANSWER 1 OF 133     MEDLINE on STN                 DUPLICATE 1
TI   Silencing Livin gene expression to inhibit proliferation and enhance
     chemosensitivity in tumor cells.

L5   ANSWER 2 OF 133     MEDLINE on STN                 DUPLICATE 2
TI   Manipulation of NK cytotoxicity by the IAP family member Livin.

L5   ANSWER 3 OF 133     MEDLINE on STN                 DUPLICATE 3
TI   Resistance of melanoma cells to TRAIL does not result from upregulation of
     antiapoptotic proteins by NF-kappaB but is related to downregulation of
     initiator caspases and DR4.

L5   ANSWER 4 OF 133     MEDLINE on STN                 DUPLICATE 4
TI   Silencing livin gene by siRNA leads to apoptosis
     induction, cell cycle arrest, and proliferation inhibition in malignant
     melanoma LiBr cells.

L5   ANSWER 5 OF 133     MEDLINE on STN                 DUPLICATE 5
TI   Expression of inhibitor of apoptosis protein Livin in
     renal cell carcinoma and non-tumorous adult kidney.
```

L5 ANSWER 6 OF 133 MEDLINE on STN DUPLICATE 6
TI Targeted inhibition of Livin resensitizes renal cancer cells towards apoptosis.

L5 ANSWER 7 OF 133 MEDLINE on STN DUPLICATE 7
TI Subcellular localization determines the delicate balance between the anti- and pro-apoptotic activity of Livin.

L5 ANSWER 8 OF 133 MEDLINE on STN DUPLICATE 8
TI Expression of apoptosis inhibitor gene Livin in bladder transitional cell carcinoma and clinical implication thereof.

L5 ANSWER 9 OF 133 MEDLINE on STN DUPLICATE 9
TI Expression of livin in gastric dancer and effect of silencing of the livin gene on apoptosis in gastric cancer cells.

L5 ANSWER 10 OF 133 MEDLINE on STN DUPLICATE 10
TI The clinical significance of autoantibodies in gastrointestinal malignancies: an overview.

L5 ANSWER 11 OF 133 MEDLINE on STN DUPLICATE 12
TI Expression of Livin, an antiapoptotic protein, is an independent favorable prognostic factor in childhood acute lymphoblastic leukemia.

L5 ANSWER 12 OF 133 MEDLINE on STN DUPLICATE 14
TI Expression patterns of inhibitor of apoptosis proteins in malignant pleural mesothelioma.

L5 ANSWER 13 OF 133 MEDLINE on STN DUPLICATE 15
TI Carboxyfullerenes localize within mitochondria and prevent the UVB-induced intrinsic apoptotic pathway.

L5 ANSWER 14 OF 133 MEDLINE on STN DUPLICATE 16
TI Livin/ML-IAP as a new target for cancer treatment.

L5 ANSWER 15 OF 133 MEDLINE on STN DUPLICATE 17
TI Expression of the apoptosis inhibitor livin in renal cell carcinomas: correlations with pathology and outcome.

L5 ANSWER 16 OF 133 MEDLINE on STN DUPLICATE 18
TI Expression of livin in renal cell carcinoma and detection of anti-livin autoantibody in patients.

L5 ANSWER 17 OF 133 MEDLINE on STN DUPLICATE 19
TI Livin/melanoma inhibitor of apoptosis protein as a potential therapeutic target for the treatment of malignancy.

L5 ANSWER 18 OF 133 MEDLINE on STN DUPLICATE 20
TI Livin promotes Smac/DIABLO degradation by ubiquitin-proteasome pathway.

L5 ANSWER 19 OF 133 MEDLINE on STN DUPLICATE 21
TI Survivin nuclear labeling index: a superior biomarker in superficial urothelial carcinoma of human urinary bladder.

L5 ANSWER 20 OF 133 MEDLINE on STN DUPLICATE 23
TI Isoform-specific silencing of the Livin gene by RNA interference defines Livin beta as key mediator of apoptosis inhibition in HeLa cells.

L5 ANSWER 21 OF 133 MEDLINE on STN DUPLICATE 24
TI Proteolytic cleavage of Livin (ML-IAP) in apoptotic melanoma cells potentially mediated by a non-canonical caspase.

L5 ANSWER 22 OF 133 MEDLINE on STN DUPLICATE 25
TI The anti-apoptotic livin gene is an important determinant for the apoptotic resistance of non-small cell lung cancer cells.

L5 ANSWER 23 OF 133 MEDLINE on STN DUPLICATE 26
TI Prognostic value of Survivin and Livin in nasopharyngeal carcinoma.

L5 ANSWER 24 OF 133 MEDLINE on STN DUPLICATE 27
TI X-Linked inhibitor of apoptosis protein expression level in colorectal cancer is regulated by hepatocyte growth factor/C-met pathway via Akt signaling.

L5 ANSWER 25 OF 133 MEDLINE on STN DUPLICATE 29
TI Survivin expression by metastatic melanoma predicts poor disease outcome in patients receiving adjuvant polyvalent vaccine.

L5 ANSWER 26 OF 133 MEDLINE on STN DUPLICATE 30
TI Aberrant expression and potency as a cancer immunotherapy target of inhibitor of apoptosis protein family, Livin/ML-IAP in lung cancer.

L5 ANSWER 27 OF 133 MEDLINE on STN DUPLICATE 31
TI Gene transfection of Livin isoforms into A549 cell line and its effect on cell growth and sensitivity to chemotherapy and radiotherapy.

L5 ANSWER 28 OF 133 MEDLINE on STN DUPLICATE 32
TI Expression of inhibitor-of-apoptosis protein (IAP) livin by neuroblastoma cells: correlation with prognostic factors and outcome.

L5 ANSWER 29 OF 133 MEDLINE on STN DUPLICATE 33
TI Selectively frequent expression of CXCR5 enhances resistance to apoptosis in CD8(+)CD34(+) T cells from patients with T-cell-lineage acute lymphocytic leukemia.

L5 ANSWER 30 OF 133 MEDLINE on STN DUPLICATE 34
TI Protein profiling and identification of modulators regulated by human papillomavirus 16 E7 oncogene in HaCaT keratinocytes by proteomics.

L5 ANSWER 31 OF 133 MEDLINE on STN DUPLICATE 35
TI CC chemokine ligand 25 enhances resistance to apoptosis in CD4+ T cells from patients with T-cell lineage acute and chronic lymphocytic leukemia by means of livin activation.

L5 ANSWER 32 OF 133 MEDLINE on STN DUPLICATE 36
TI Telomere-based DNA damage responses: a new approach to melanoma.

L5 ANSWER 33 OF 133 MEDLINE on STN DUPLICATE 37
TI The melanoma inhibitor of apoptosis protein: a target for spontaneous cytotoxic T cell responses.

L5 ANSWER 34 OF 133 MEDLINE on STN DUPLICATE 38
TI Expression of survivin mRNA and livin mRNA in non-small-cell lung cancer.

L5 ANSWER 35 OF 133 MEDLINE on STN DUPLICATE 39
TI Inhibition of apoptosis in normal and transformed intestinal epithelial cells by cAMP through induction of inhibitor of apoptosis protein (IAP)-2.

L5 ANSWER 36 OF 133 MEDLINE on STN DUPLICATE 40
TI Induction of apoptosis in tumor cells by siRNA-mediated silencing of the livin/ML-IAP/KIAP gene.

L5 ANSWER 37 OF 133 MEDLINE on STN DUPLICATE 42
TI Temporal and spatial patterns of expression of inhibitors of apoptosis in human placentas.

L5 ANSWER 38 OF 133 MEDLINE on STN DUPLICATE 43
TI Expression and prognostic significance of LIVIN, SURVIVIN and other apoptosis-related genes in the progression of superficial bladder cancer.

L5 ANSWER 39 OF 133 MEDLINE on STN DUPLICATE 44
TI Apoptosis regulators and responses in human melanocytic and keratinocytic cells.

L5 ANSWER 40 OF 133 MEDLINE on STN DUPLICATE 45
TI Expressed sequence tag analysis of adult human lens for the NEIBank Project: over 2000 non-redundant transcripts, novel genes and splice variants.

L5 ANSWER 41 OF 133 MEDLINE on STN DUPLICATE 46
TI Livin, a novel inhibitor of apoptosis protein family member.

L5 ANSWER 42 OF 133 MEDLINE on STN DUPLICATE 47
TI Two splicing variants of a new inhibitor of apoptosis gene with different biological properties and tissue distribution pattern.

L5 ANSWER 43 OF 133 MEDLINE on STN
TI Expression and prognostic significance of Livin in the progression of bladder cancer.

L5 ANSWER 44 OF 133 MEDLINE on STN
TI Expression of anti-apoptosis livin gene in acute non-lymphocytic leukemia cells and its clinical significance.

L5 ANSWER 45 OF 133 MEDLINE on STN
TI Expression of apoptosis inhibitor gene Livin in prostate cancer and its clinical implication.

L5 ANSWER 46 OF 133 MEDLINE on STN
TI Expression and clinical significance of Survivin and Livin in DukesoB colorectal cancer.

L5 ANSWER 47 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Expression of the inhibitor of apoptosis livin in testicular germ cell tumours: Correlations with clinicopathological tumour features.

L5 ANSWER 48 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Linvin, a novel inhibitor of apoptosis protein.

L5 ANSWER 49 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Expression of livin, a novel member of the inhibitor-of-apoptosis protein (IAP) family, in neuroblastoma: Possible prognostic significance.

L5 ANSWER 50 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Livin expression in normal hematopoietic cells and in hematologic

malignancies.

L5 ANSWER 51 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Expression of inhibitor-of-apoptosis protein (IAP) livin in pediatric acute lymphoblastic leukemia (ALL) cells.

L5 ANSWER 52 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Expression of inhibitor-of-apoptosis protein livin by neuroblastoma cells: Correlation with stage of cellular maturation.

L5 ANSWER 53 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Livin, a novel member of inhibitor of apoptosis, is marker of poor prognosis in gastric cancer.

L5 ANSWER 54 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Sub-cellular localization determines the delicate balance between the anti and proapoptotic activity of Livin.

L5 ANSWER 55 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Livin, an inhibitor of apoptosis family member is a novel target for cancer immunotherapy.

L5 ANSWER 56 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Apoptotic cleavage of livin in melanoma cells.

L5 ANSWER 57 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Caspase-mediated cleavage paradoxically converts Livin from an anti-apoptotic to a pro-apoptotic factor: Implications for CLL, AML and drug resistant melanoma.

L5 ANSWER 58 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Apoptosis and melanoma: Molecular mechanisms.

L5 ANSWER 59 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Differences in Gene Regulation among Members of the IAP Family in Response to Activation of Hematopoietic Cells.

L5 ANSWER 60 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Effector but Not Initiator Caspases Cleave the Inhibitor of Apoptosis Protein "Livin".

L5 ANSWER 61 OF 133 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Livin, a new inhibitor of apoptosis protein, is expressed at high levels in some chronic lymphatic leukemia (CLL) patients, and may contribute to the apoptotic defect in low grade hematological malignancies.

L5 ANSWER 62 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 11
TI Expression of livin in lung cancer tissue and its relationship with the expression of caspase-3

L5 ANSWER 63 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 13
TI Study on enhancing sensitivity of SPC-A1 cells to chemotherapy by Livin isoform-specific gene silencing

L5 ANSWER 64 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 22
TI The expression and clinical significance of Livin in non-small cell lung cancer

L5 ANSWER 65 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 28
TI Apoptosis of nasopharyngeal carcinoma cells induced by inhibitors of topoisomerase II, ADM and THP

L5 ANSWER 66 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 41
TI Livin - potential target for cancer treatment

L5 ANSWER 67 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Inhibitor of apoptosis protein Livin

L5 ANSWER 68 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression and significance of inhibitor of apoptosis protein Livin in oral squamous cell carcinoma and precancerous lesion

L5 ANSWER 69 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Enhancement of humanized immunoglobulin expression in transgenic animals through suppression of B-cell apoptosis

L5 ANSWER 70 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Degradation of Survivin by the X-linked Inhibitor of Apoptosis (XIAP)-XAF1 Complex

L5 ANSWER 71 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Effects of proanthocyanidins on the expression of gene livin and caspase-3 in cervical cancer Hela cell

L5 ANSWER 72 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of Livin gene and its isoforms in children with gliomas

L5 ANSWER 73 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of inhibitor-of-apoptosis protein family members in malignant mesothelioma

L5 ANSWER 74 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Association of expression of livin, Bcl-2 and p53 gene in cervical carcinoma

L5 ANSWER 75 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of inhibitor of apoptosis protein livin in human primary hepatocellular carcinoma cell HEPG-2

L5 ANSWER 76 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of livin gene and protein in breast carcinoma and its relationship with cell proliferation and apoptosis

L5 ANSWER 77 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression and its significance of the apoptotic inhibitor Livin and Survivin in breast cancer

L5 ANSWER 78 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Inhibitor of apoptosis proteins are regulated by tumour necrosis factor-α in malignant pleural mesothelioma

L5 ANSWER 79 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN

TI Inhibitor of apoptosis protein Livin and lung cancer

L5 ANSWER 80 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of Livin in breast carcinoma and its relationship with Caspase-3 and Ki67

L5 ANSWER 81 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Construction of prokaryotic expression vectors for livin alpha and livin beta

L5 ANSWER 82 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Survivin, a member of the inhibitors of apoptosis family, is down-regulated in breast carcinoma effusions

L5 ANSWER 83 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of Livin mRNA and protein in human oral squamous cell carcinoma

L5 ANSWER 84 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of Livin mRNA and Livin protein in esophageal carcinoma

L5 ANSWER 85 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Nuclear expression of survivin is associated with improved survival in metastatic ovarian carcinoma

L5 ANSWER 86 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of livin in benign and malignant endometrial diseases

L5 ANSWER 87 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI The role of IAP as a novel diagnostic and therapeutic target for prostate cancer

L5 ANSWER 88 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Livin and digestive tract carcinoma

L5 ANSWER 89 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression-analysis of apoptosis-associated genes in pancreatic ductal adenocarcinoma

L5 ANSWER 90 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Genes showing altered levels of expression in breast cancer and their use in diagnosis and prognosis and in selection of therapies

L5 ANSWER 91 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Use of peptides derived from SMAC proteins to stimulate autodegradation of cellular inhibitors of apoptosis

L5 ANSWER 92 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Detection of autoantibodies against cancer antigens

L5 ANSWER 93 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Recent research about Livin in cancer

L5 ANSWER 94 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression and clinical significance of inhibitor-of-apoptosis Livin in laryngeal squamous carcinoma

L5 ANSWER 95 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of apoptosis inhibiting protein livin in non-small cell lung cancer and its clinical significance

L5 ANSWER 96 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Apoptosis and proliferation markers in diffusely infiltrating

astrocytomas: profiling of 17 molecules

L5 ANSWER 97 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of inhibitor of apoptosis protein Livin in papilloma tissue of larynx

L5 ANSWER 98 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression levels and difference of anti-apoptotic genes livin and survivin in breast cancer

L5 ANSWER 99 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of livin in human brain gliomas and its biological significance

L5 ANSWER 100 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI The research of the expression of stress-induced caspase-3 and livin in early pregnant placental tissues

L5 ANSWER 101 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of inhibitor of apoptosis protein livin in transitional cell carcinoma of bladder

L5 ANSWER 102 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of livin, a novel inhibitor of apoptosis protein family member, in tissues of gastric cancer

L5 ANSWER 103 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Construction of Livin isoform-specific siRNA expression vector and its stable expression in SPC-A1 cells

L5 ANSWER 104 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Livin gene overexpression and tumor drug resistance

L5 ANSWER 105 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Livin in cancer development

L5 ANSWER 106 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expression of livin and survivin in human gastric carcinoma

L5 ANSWER 107 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Genes regulated by carbon source in the colon and their use in the early diagnosis of colon cancer

L5 ANSWER 108 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI HLA-A24 binding cancer antigen peptides derived from human livin and use as cancer vaccine and in cancer diagnosis

L5 ANSWER 109 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Construction of eukaryotic expression vectors for Livin alpha and beta

L5 ANSWER 110 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Inhibitor of apoptosis livin and its clinical significance

L5 ANSWER 111 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Bone marrow cells of myelodysplastic syndromes exhibit significant expression of apollon, livin and ILP-2 with reduction after transformation to overt leukemia

L5 ANSWER 112 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Transfection of gene livin α/β into A549 cells and separate effect on the cell growth

L5 ANSWER 113 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Detection of autoantibodies to survivin and livin in sera from patients with breast cancer

L5 ANSWER 114 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Livin-derived pro-apoptotic peptides for induction of apoptosis and tumor therapy

L5 ANSWER 115 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Serine protease Omi mutants and genes and methods for modulating Inhibitor of Apoptosis activity and treatment of diseases

L5 ANSWER 116 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI DNA vaccines encoding IAP or inhibitor of apoptosis proteins and cytokine or ligand of NK cell surface receptor for cancer therapy

L5 ANSWER 117 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Antisense modulation of livin expression

L5 ANSWER 118 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI SiRNA targeting inhibitor of apoptosis protein livin for treatment of therapy-resistant tumors

L5 ANSWER 119 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Peptides for inducing apoptosis in tumor cells

L5 ANSWER 120 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Smac/DIABLO Selectively Reduces the Levels of c-IAP1 and c-IAP2 but Not That of XIAP and Livin in HeLa Cells

L5 ANSWER 121 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Novel inhibitor of apoptosis: livin

L5 ANSWER 122 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Telomere-based DNA damage responses: a new approach to melanoma

L5 ANSWER 123 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Potent general cancer vaccines targeting inhibitor of apoptosis proteins

L5 ANSWER 124 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Rapid induction of mitochondrial events and caspase-independent apoptosis in Survivin-targeted melanoma cells

L5 ANSWER 125 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Methods and reagents for peptide-BIR interaction screens

L5 ANSWER 126 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Caspase-Mediated Cleavage Converts Livin from an Antiapoptotic to a Proapoptotic Factor: Implications for Drug-Resistant Melanoma

L5 ANSWER 127 OF 133 CAPLUS COPYRIGHT 2008 ACS on STN
TI Protein and cDNA sequences of a novel human livin gene: inhibitor-of-apoptosis protein-3 (IAP-3) and its therapeutic uses

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TI Effect of gene livin transfection on the proliferation and apoptosis in bladder carcinoma cells.

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TI Induction of apoptosis in SGC-7901 cells by small interfering RNA-mediated silencing of the livin gene.

L5 ANSWER 130 OF 133 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Study of livin and tumor apoptosis.

L5 ANSWER 131 OF 133 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Effects of the proliferation and apoptosis of mammary cancer MCF-7 cells by antisense oligodeoxynucleotides against inhibitor of apoptosis protein Livin.

L5 ANSWER 132 OF 133 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Expression of a novel inhibitor of apoptosis protein livin in malignant tumor cells and tissues and its clinical significance.

L5 ANSWER 133 OF 133 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Expression and clinical significance of livin in human astrocytoma.

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L1            59 S LIVIN (S) APOPTO? AND PD<=20040531
L2            32 DUP REM L1 (27 DUPLICATES REMOVED)
L3             0 S L2 AND (P30 OR P28)
L4           243 S LIVIN(S) APOPTO?
L5           133 DUP REM L4 (110 DUPLICATES REMOVED)

=> D Ibib abs L5 7, 20, 21, 27, 42

L5   ANSWER 7 OF 133     MEDLINE on STN                DUPLICATE 7
ACCESSION NUMBER:   2007343871     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 17294084
TITLE:              Subcellular localization determines the delicate balance
                    between the anti- and pro-apoptotic activity of
                    Livin.
AUTHOR:             Nachmias Boaz; Lazar Itay; Elmalech Meital; Abed-El-Rahaman
                    Ihab; Asshab Yaqoub; Mandelboim Ofer; Perlman Riki;
                    Ben-Yehuda Dina
CORPORATE SOURCE:   Department of Hematology, Hadassah - Hebrew University
                    Medical Center, P.O.B. 12000, Jerusalem, 91120, Israel.
SOURCE:             Apoptosis : an international journal on programmed cell
                    death, (2007 Jul) Vol. 12, No. 7, pp. 1129-42.
                    Journal code: 9712129. ISSN: 1360-8185.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200711
ENTRY DATE:         Entered STN: 12 Jun 2007
                    Last Updated on STN: 14 Nov 2007
                    Entered Medline: 13 Nov 2007
AB   Livin is a member of the Inhibitor of Apoptosis
     Protein family which inhibits apoptosis induced by a variety of
     stimuli.  We previously identified Livin and demonstrated that
     following apoptotic stimuli, Livin is cleaved by
     effector caspases to produce a truncated form with paradoxical pro-
     apoptotic activity.  In the present study, we reveal that while
     full-length Livin shows diffuse cytoplasmic localization, truncated Livin
     (tLivin) is found in a peri-nuclear distribution with marked localization
     to the Golgi apparatus.  Using mutation analysis, we identified two
     domains that are crucial for the pro-apoptotic activity of tLivin: the
     N-terminal region of tLivin which is exposed by cleavage, and the RING
     domain.  We demonstrate that, of the N-terminal sequence, only the first
     N-terminal glycine residue dictates the peri-nuclear distribution of
     tLivin.  However, while the perinuclear localization of tLivin is
     essential, it is not sufficient for tLivin to exert its pro-apoptotic
     function.  Once tLivin is properly localized, an intact RING domain
     enables its pro-apoptotic function.

L5   ANSWER 20 OF 133     MEDLINE on STN                DUPLICATE 23
ACCESSION NUMBER:   2006114350     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 16437214
TITLE:              Isoform-specific silencing of the Livin gene by
                    RNA interference defines Livin beta as key
                    mediator of apoptosis inhibition in HeLa cells.
AUTHOR:             Crnkovic-Mertens Irena; Semzow Julia; Hoppe-Seyler Felix;
                    Butz Karin
CORPORATE SOURCE:   Deutsches Krebsforschungszentrum, Molekulare Therapie
                    Virus-Assoziierter Tumore (F065), Im Neuenheimer Feld 242,
                    69120, Heidelberg, Germany.. k.butz@dkfz.de
SOURCE:             Journal of molecular medicine (Berlin, Germany), (2006 Mar)
                    Vol. 84, No. 3, pp. 232-40.  Electronic Publication:
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2005-12-31.
Journal code: 9504370. ISSN: 0946-2716.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200608
ENTRY DATE: Entered STN: 28 Feb 2006
Last Updated on STN: 31 Aug 2006
Entered Medline: 30 Aug 2006

AB Livin (alternatively called ML-IAP or KIAP) is a cancer-associated member of the antiapoptotic inhibitor of apoptosis protein family. Two splicing variants of Livin, designated Livin alpha and Livin beta, have been identified. The significance of these isoforms for Livin-mediated apoptosis inhibition is largely unclear. Using an isoform-specific RNA interference (RNAi) strategy, we silenced endogenous Livin expression in HeLa cells. We found that the targeted inhibition of Livin beta, but not of Livin alpha, blocked the growth of HeLa cells in clonogenic survival assays. In addition, silencing of Livin beta, but not of Livin alpha, sensitized HeLa cells to different proapoptotic stimuli such as UV irradiation, tumor necrosis factor alpha, or etoposide. These events were linked to activation of caspase-3 and increased poly(ADP-ribose) polymerase cleavage, specifically upon silencing of Livin beta. The proapoptotic sensitization of HeLa cells upon RNAi-mediated silencing of the endogenous livin gene was specifically reverted by ectopic expression of Livin beta but not of Livin alpha. We conclude that the Livin beta isoform plays the key role for the antiapoptotic protection of HeLa cells by the livin gene. Our results show that the Livin isoforms can strongly differ in their functional significance for the antiapoptotic resistance of tumor cells. Studies evaluating Livin as a novel diagnostic and prognostic tumor marker should benefit from isoform-specific expression analyses.

L5 ANSWER 21 OF 133 MEDLINE on STN DUPLICATE 24
ACCESSION NUMBER: 2006481211 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16806840
TITLE: Proteolytic cleavage of Livin (ML-IAP) in apoptotic melanoma cells potentially mediated by a non-canonical caspase.
AUTHOR: Yan Hui; Brouha Brook; Liu Tong; Raj Deepak; Biddle Diana; Lee Ray; Grossman Douglas
CORPORATE SOURCE: Huntsman Cancer Institute, University of Utah, Suite 5243, 2000 Circle of Hope, Salt Lake City, UT 84112, USA.
CONTRACT NUMBER: AR050102 (United States NIAMS)
R01 AR050102-03 (United States NIAMS)
SOURCE: Journal of dermatological science, (2006 Sep) Vol. 43, No. 3, pp. 189-200. Electronic Publication: 2006-06-27.
Journal code: 9011485. ISSN: 0923-1811.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 15 Aug 2006
Last Updated on STN: 24 Oct 2006
Entered Medline: 24 Oct 2006

AB BACKGROUND: Several inhibitor of apoptosis proteins (IAPs) are cleaved during apoptosis. Studies of the melanoma-associated IAP (ML-IAP) Livin,

using recombinant molecules, have implicated both caspases 3/7 and the serine protease Omi/HtrA2 in its proteolytic cleavage. OBJECTIVE: To characterize the apoptotic cleavage of Livin in melanocytic cells, and evaluate the role of known proteases. METHODS: We assessed the capacity of a variety of stimuli to induce Livin cleavage in human melanoma cell lines and normal human melanocytes. The role of caspases and Omi was examined using caspase inhibitors and RNAi, respectively. A potential caspase substrate was further examined by site-directed mutagenesis. Deletion mapping was used to identify the cleavage site. RESULTS: Livin cleavage was observed in multiple human melanoma cell lines in response to a variety of apoptotic stimuli (UVB, 4-TBP, cisplatin, TNF, Bax), and not affected by the addition of various protease inhibitors or RNAi-mediated silencing of Omi/HtrA2. Livin cleavage induced by 4-TBP, but not UVB or cisplatin, was blocked by the pan-caspase inhibitor zVAD-fmk. Mutation of Asp52 to Glu in Livin did not affect cleavage, while either mutation of Asp52 to Ala, deletion of Asp52, or deletion of the adjacent region (residues 53-61) abrogated cleavage. CONCLUSION: Livin cleavage, induced by multiple apoptotic stimuli in melanoma cells, likely occurs in an Omi-independent fashion at residue 52 within its potential caspase substrate (DHVD52). However, relative insensitivity of the apoptotic cleavage to zVAD-fmk, or Asp52 to Glu mutation, suggests the involvement of a non-canonical caspase.

L5 ANSWER 27 OF 133 MEDLINE on STN DUPLICATE 31
ACCESSION NUMBER: 2006024103 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 16409786
TITLE: Gene transfection of Livin isoforms into A549 cell line and its effect on cell growth and sensitivity to chemotherapy and radiotherapy.
AUTHOR: Sun Jian-guo; Liao Rong-xia; Chen Zheng-tang; Wang Zhi-xin; Zhang Qing; Hu Yi-de; Wang Dong-lin
CORPORATE SOURCE: Cancer Center of PLA, Xinqiao Hospital, Third Military Medical University, Chongqing 400037, China.
SOURCE: Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases, (2005 Dec) Vol. 28, No. 12, pp. 836-40. Journal code: 8712226. ISSN: 1001-0939.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 14 Jan 2006 Last Updated on STN: 12 Dec 2006
AB OBJECTIVE: To express Livin alpha & beta in A549 cells by using gene transfection, and to observe its effect on cell growth and cell sensitivity to chemotherapy drugs and radiation. METHODS: Eukaryotic expression vectors of Livin alpha & beta were transfected into A549 cells and cell clones with stable expression were obtained. Livin alpha & beta expression levels in the transfected A549 cells were assessed at mRNA level and protein level, respectively. Cell growth status was assessed by biological features. MTT was performed to test effects of Livin on sensitivity of the A549 cells to chemotherapy drugs and radiation, and cell cycle analysis was performed to evaluate cell apoptosis. RESULTS: After transfection, positive cells, especially A549 cells expressing Livin, showed an increase of about 20% in colony-forming ability, a shorter doubling time ($P < 0.05$) and lower sensitivity to chemotherapy drugs and radiation ($P < 0.01$). Only 0.2% of the cells committed apoptosis with 10 Gy radiation. CONCLUSION: Livin isoforms, especially Livin alpha, are implicated in genesis and development of lung cancer, thus may be an important mechanism for drug resistance of lung

cancer cells.

L5 ANSWER 42 OF 133 MEDLINE on STN DUPLICATE 47
ACCESSION NUMBER: 2001271909 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11322947
TITLE: Two splicing variants of a new inhibitor of apoptosis gene with different biological properties and tissue distribution pattern.
AUTHOR: Ashhab Y; Alian A; Polliack A; Panet A; Ben Yehuda D
CORPORATE SOURCE: Department of Hematology, Hadassah University Hospital, Ein-Karem, P.O. Box 12000, Jerusalem 91120, Israel.
SOURCE: FEBS letters, (2001 Apr 20) Vol. 495, No. 1-2, pp. 56-60. Journal code: 0155157. ISSN: 0014-5793.
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AB Using homology searches, we identified a novel human inhibitor of apoptosis (IAP) gene. This gene has two splicing variants that contain open reading frames of 298 and 280 amino acids and both contained a single copy of baculovirus IAP repeat (BIR) and RING domain. We refer here to the longer and shorter variants as Livin alpha and beta, respectively. Semiquantitative reverse transcriptase-polymerase chain reaction demonstrated a tissue-specific and non-correlated expression pattern in both adult and fetal tissues. Both mRNA variants were detected in various transformed cell lines. Despite their very close similarity, the two isoforms have different antiapoptotic properties. Both isoforms have a significant antiapoptotic activity in the Jurkat T cell line after triggering apoptosis via tumor necrosis factor and CD95 receptors. The Livin alpha but not beta protects cells from apoptosis induced by staurosporine, but in contrast, apoptosis initiated by etoposide was blocked only by the beta isoform. This difference in biological activities may indicate the presence of critical amino acids outside the BIR and RING domains. These functional and tissue distribution differences of Livin alpha and beta suggest that Livin may play a complex role in the regulation of apoptosis.

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